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Introduction

Background

This report provides reference information for blood or urine concentrations of 27 biochemical indicators of diet and nutrition measured by the Centers for Disease Control and Prevention (CDC), Division of Laboratory Sciences at the National Center for Environmental Health (NCEH/DLS). The indicators were measured in specimens from a representative sample of the noninstitutionalized civilian U.S. population during all or part of the four-year period from 1999 through 2002. These specimens were collected by CDC's National Health and Nutrition Examination Survey (NHANES), which is conducted by CDC's National Center for Health Statistics (NCHS). NHANES is a series of surveys designed to collect data on the health and nutritional status of the U.S. population. This report covers one important facet in the assessment of nutritional status of the U.S. population: biochemical measurements. Other aspects, such as anthropometric body measurements, hematologic measurements, clinical signs of nutritional deficiency or excess, and dietary intake, are not covered.

For this report, a biochemical indicator means a vitamin, iron-status indicator, trace element, or other dietary indicator with potential health relevance. Although most biochemical indicators presented in this report enter the human body from foods or supplements, the body itself produces some indicators in response to dietary intake. Blood and urine concentrations reflect the amount of nutrients and dietary compounds actually in the body from all of these sources.

The biochemical indicators covered in this report are:

- Water-soluble vitamins and related biochemical compounds.
- Fat-soluble vitamins and micronutrients.
- Iron-status indicators.
- Trace elements.
- Isoflavones and lignans (so-called phytoestrogens).

Some indicators covered in this report have no nutritional value (e.g., homocysteine, methylmalonic acid, iron-status indicators, phytoestrogens). Yet, they are important because 1) they reflect micronutrient or metabolic status or 2) because they are a naturally occurring ingredient in the human diet (i.e., they are consumed as food or as dietary supplements) and have been associated with potential positive or negative health outcomes.

On the other hand, some important micronutrients, such as vitamin C, vitamin B6, or certain minerals (e.g., sodium, potassium, calcium, phosphorus, chloride, magnesium) are omitted from this report. Data were either unavailable for the report years covered or were not representative of micronutrient status. Future reports may, however, include other biochemical indicators of diet and nutrition.

Addressing Data Needs

This report is CDC's first product that presents data—in a single source—concerning NCEH/DLS measurements of a wide range of biochemical indicators of diet and nutrition from the most recent continuous NHANES survey, starting in 1999.

NCHS has historically released or commissioned a variety of products presenting NHANES results. Among these are Data Briefs, Data Tables, Advance Data, Series Reports, and Reports through the Life Sciences Research Office (LSRO). See the following for further information: http://www.cdc.gov/nchs/about/major/nhanes/survey_results_and_products.htm.

NHANES Series Reports (mainly Series 11) and LSRO Reports have always been of particular value to the nutrition community (see Appendix A). The two latest reports on nutritional biochemistry reference data were prepared for NHANES III (1988–1994). One covered hematologic and iron-related analytes, and the other covered blood folate and vitamin B12.

Public Health Uses

The primary purpose of this report is to improve our understanding of the concentrations of biochemical indicators of diet and nutrition in the general U.S. population and in selected subpopulations. These data will help assess inadequate or excess intake and will inform analyses on the relation between biochemical indicators and health outcomes. Other potential public health uses of the information include the following:

- Establishing and improving upon existing population reference levels that physicians, clinicians, scientists, and public health officials can use to determine whether a person or a group of people has an unusually high or low level of a biochemical indicator of diet and nutrition.
- Determining whether the nutritional status of special population groups, such as minorities, children, women of childbearing age, or the elderly is different from that of other groups, or whether it needs improvement.
- Tracking, over time, trends in biochemical indicator levels in the population.
- Assessing the effectiveness of public health efforts to improve the diet and nutritional status of U.S. residents.
- Stimulating research to perform more in-depth analyses of the NHANES data and to generate hypotheses for future nutrition and human health studies.

Data Presented for Each Biochemical Indicator

This publication contains tables of descriptive statistics on the distribution of blood and urine concentrations for each biochemical indicator of diet and nutrition. Statistics include unadjusted geometric means and selected percentiles with confidence intervals.

The data are grouped by age, sex, and race/ethnicity. A geometric mean provides a better estimate of central tendency for data distributions with a long tail at the upper end of the distribution. When measuring biochemical indicators, this type of distribution is common. The geometric mean is influenced less by high values than is the arithmetic mean. Scientists can use the presented percentile levels (5th or 10th, 50th, and 90th or 95th) to determine which serum, blood, or urine concentrations of indicators are common to people in the U.S. population and which concentrations are unusual. We used the unweighted sample size as a criterion for indicating reliable results (U.S. Centers for Disease for Control and Prevention 1996, Appendix B, Table 1). We assumed an average design effect of 1.4 and used a sample size of at least 112 persons to define estimates for the 10th and 90th percentiles as reliable and a sample size of at least 224 persons to define estimates for the 5th and 95th percentiles as reliable. We present 10th and 90th percentile levels for a biochemical indicator when the sample size was too small for 5th and 95th percentile levels in several subgroups. This is the case after stratifying by age, sex, and race/ethnicity with data from only two years (carotenoids, 25-hydroxyvitamin D, some iron-status indicators) or with data from only a subset of the population (iodine, selenium, phytoestrogens). For urine measurements, data are shown for both the concentration and for the concentration corrected for the urinary creatinine level.

General information is provided for each indicator that also aids in interpreting levels.

To address sources of these nutrients, biochemical pathways in the body, and known health effects, the text contains a brief overview about each indicator.

Selected observations and highlights—mainly derived from the data tables provided in this publication—are presented in each chapter.

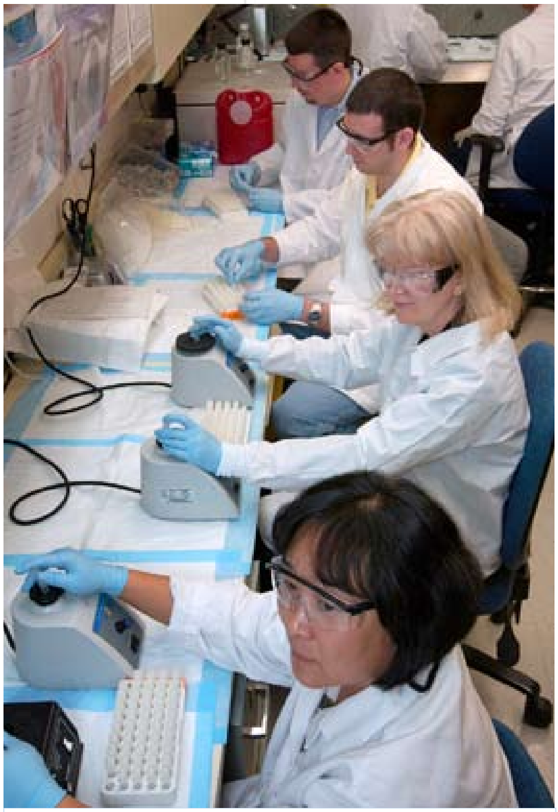
The observations describe categorical differences between demographic subgroups, whereas the highlights summarize the observations in a public health context.

Interpreting the Data

Adequate serum or blood concentrations of biochemical indicators do not necessarily indicate that NHANES participants consume healthful and balanced diets. Some foods are fortified with micronutrients (e.g., iron, thiamin, riboflavin, niacin, folate, vitamin A, vitamin D), and some people take dietary supplements that contain vitamins, minerals, or both.

Although certain dietary deficiencies are well documented and have characteristic signs and symptoms, suboptimal concentrations have been associated with the risk for adverse health effects such as cardiovascular disease, stroke, impaired cognitive function, cancer, eye diseases, poor bone health, and other conditions. Adverse health effects, including toxicity, are also possible from consuming excess amounts of certain nutrients. Research studies, separate from this report, are required to determine those concentrations of a biochemical indicator that may indicate risk for disease and those concentrations that are of negligible health concern. In collaboration with other agencies and institutions, CDC encourages, and itself conducts, measurements for this type of research.

This report contains unadjusted geometric means and selected percentiles of biochemical indicators of diet and nutrition for the civilian, noninstitutionalized U.S. population. A limited interpretation of relative differences between population groups is possible by identifying groups with non-overlapping confidence intervals. These observed differences, however, should not be interpreted as causal. The intent is to describe the characteristics of the population and of selected subgroups, and not to explain why the groups look the way they do or why they differ from each other. For example, for biochemical indicators correlated with age, age may account for some of the effects. Furthermore, differences in biochemical indicator concentrations of selected subgroups do not necessarily imply health problems. More in-depth statistical analyses, such as adjusting for demographic variables or covariates, and taking interactions or predictive variables into consideration, are beyond the scope of this publication. We hope nonetheless that scientists will be stimulated to examine the data further by analyzing the raw data available at this Web site: http://www.cdc.gov/nchs/nhanes.htm.



Chemists prepare serum material for quality assurance.

Laboratories may use different methods for measuring the indicators reported here. Different methods may result in different method-specific reference ranges. Consequently, to apply these results, health science professionals should check with their particular laboratory to be sure their methods compare closely with those used in this report (see Appendix B).

Useful Sources of Information about Using Nutrition Monitoring to Interpret Data

Information about dietary intake is critical to research examining the reasons for nutritional inadequacies and for programs to improve diet and nutritional status. Selected NCHS Advance Data Reports provide useful overviews (see Appendix A). Also of value are the U.S. Department of Agriculture's (USDA) databases on food surveys and food composition:

What We Eat in America (WWEIA) is the dietary intake interview section of NHANES (http://www.ars.usda.gov/foodsurvey).

The Food and Nutrient Database for Dietary Studies (FNDDS) (http://www.ars.usda.gov/Services/docs.htm?docid=12089) is a database of foods, their nutrient values, and weights for typical food portions. This database helps to analyze data from the WWEIA survey by using the nutrient values from the National Nutrient Database for Standard Reference (http://www.ars.usda.gov/Services/docs.htm?docid=8964).

The Directory of Federal and State Nutrition Monitoring and Related Research Activities (Interagency Board for Nutrition Monitoring and Related Research 2000) is the fourth update in a series that provides information on the complex system of nutrition monitoring in the United States. It is a guide to those federal and state survey, surveillance, and research activities that are part of the National Nutrition Monitoring and Related Research Program (http://www.cdc.gov/nchs/about/otheract/nutrishn/nutrishn.htm).

The Third Report on Nutrition Monitoring in the United States (Interagency Board for Nutrition Monitoring and Related Research 1995) provides the latest update on the dietary, nutritional, and nutrition-related health status of United States residents, the relation between diet and health, and the factors that influence dietary and nutritional status.

The National Health and Nutrition Examination Survey (NHANES)

CDC laboratory scientists used biological specimens obtained from participants in NHANES to measure biochemical indicators of diet and nutrition for this publication. NHANES is a series of NCHS-conducted surveys designed to collect data on the health and nutritional status of the U.S. population. This is the only national survey that collects biological samples. The NHANES surveys began in 1960 with the fielding of the first Health Examination Survey (HES 1). The nutritional component was added in the early 1970s in NHANES I. In 1999 NHANES became a continuous survey, sampling the U.S. population annually and releasing the data in two-year cycles.

NHANES collects information on a wide range of health-related behaviors, conducts physical examinations, and collects samples for laboratory tests. Because of physical examination and biological measures, NHANES is unique in its ability to examine public health issues, such as risk factors for cardiovascular disease, in the U.S. population. To select a representative sample of the civilian, noninstitutionalized population in the United States, the survey sampling plan follows a complex, stratified, multistage, probability-cluster design. The civilian, noninstitutionalized population consists of persons who are neither in the military nor institutionalized (e.g., residents of nursing homes, college dormitories, or prisons).

The NHANES protocol includes a home interview followed by a standardized physical examination at a mobile examination center. As part of the examination, for participants aged 1 year and older, blood is obtained by venipuncture. Urine specimens are collected from participants aged 6 years and older. By design, approximately half of the participants are evaluated after an overnight fast. Furthermore, close to 90 percent of all participants have fasted for more than 3 hours before providing a biological sample. Because the mobile examination centers can be adversely affected by weather, data are collected in northern latitudes in summer and in southern latitudes in winter. This seasonal-latitude structure might indirectly affect biochemical indicators.

Additional detailed information about the design and conduct of the NHANES survey is available at: http://www.cdc.gov/nchs/nhanes.htm. Information about how biological specimens are collected is available at the following Web site: http://www.cdc.gov/nchs/data/nhanes/blood.pdf and in the Laboratory Procedures Manual, which can be found at: http://www.cdc.gov/nchs/data/nhanes/lab1-6.pdf or at http://www.cdc.gov/nchs/data/nhanes/lab7-11.pdf.

Data Analysis

NCHS has developed a comprehensive Web-based tutorial (http://www.cdc.gov/nchs/tutorials/Nhanes/index.htm) to help users better understand the complex survey design and to help them analyze continuous NHANES data.

Because the NHANES sample design is complex, sample weights adjust for the unequal probability of selection into the survey. Sample weights also adjust for possible bias resulting from nonresponse and are post-stratified to U.S. Census Bureau estimates of the U.S. population. Data were analyzed using the statistical software package Statistical Analysis System (SAS) (SAS Institute Inc., 2002) and the statistical software package SUDAAN (SUDAAN Release 8.0, 2001). SUDAAN uses sample weights and calculates variance estimates that account for the complex survey design. Guidelines for the analysis of NHANES data are provided by NCHS at: http://www.cdc.gov/nchs/about/major/nhanes/nhanes2003-2004/analytical_guidelines.htm. Variance estimates were calculated using the Taylor series (linearization) method within SUDAAN. The Korn and Graubard method was used to compute Clopper-Pearson 95 percent confidence intervals (see Appendix C).

The tables show selected percentiles and unadjusted geometric means of analyte concentrations. Geometric means were calculated by taking the log of each concentration, calculating the mean of those log values, then taking the antilog of that mean (the calculation can be done using any log base, such as 10 or e). Percentile estimates were calculated using SAS Proc Univariate with weighted data. Results are shown for the total population and also by age group, sex, and race/ethnicity as defined in NHANES. For these analyses, sex is coded as male or female, and race/ethnicity is categorized as Mexican American, non-Hispanic black, and non-Hispanic white. Other racial or ethnic groups are sampled, but the proportion of the total population represented by these other groups is not large enough to produce valid estimates. Other racial/ethnic groups are included in estimates based on the entire population sample. Data for each racial/ethnic group are presented in three separate tables.

For calculation of geometric means, concentrations less than the limit of detection (LOD) were assigned a value equal to the LOD divided by the square root of 2. The LOD is the level at which the measurement has a 95 percent probability of being greater than zero (Taylor 1987). By comparison, assigning a value of the LOD divided by 2 made little difference in geometric mean estimates. Percentile estimates less than the LOD for the nutritional indicators are reported as "< LOD." If the proportion of results below the LOD was greater than 40 percent, geometric means were not calculated. Appendix D contains a table of LOD values for each biochemical indicator. As a result of changes to analytical methods, even for the same indicator, LOD values may change over the time period of the report. This was the case only for urinary phytoestrogens. We used the higher of the two LOD values for the analysis of the combined four-year data.

For biochemical indicators measured in urine, we present separate tables for the concentration of the indicator expressed as “per volume of urine” (uncorrected table) and the concentration of the indicator expressed as “per gram of creatinine” (creatinine-corrected table). Comparison of an individual participant’s result to population data in the tables requires correction for urinary dilution: thus, an individual creatinine-corrected result is best compared to the creatinine-corrected data tables. Study populations of sufficient size can be compared to the tables having either of the corresponding units. We used the uncorrected tables to compare urine concentrations across groups. Because instrument responses are measured in units of weight per volume, LOD calculations were performed using the concentration of the indicator expressed as per volume of urine. For this reason, LOD results for urine measurements in Appendix D are in weight per volume of urine. In the creatinine-corrected tables, a result for a geometric mean or percentile was reported as less than the LOD (< LOD) if the corresponding geometric mean or percentile was < LOD in the uncorrected table. Thus, for example, if the 5th percentile for males was < LOD in the uncorrected table, it would also be < LOD in the creatinine-corrected table.

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